Working Document Not for Implementation

Stability Review Tool Introduction

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Requirement

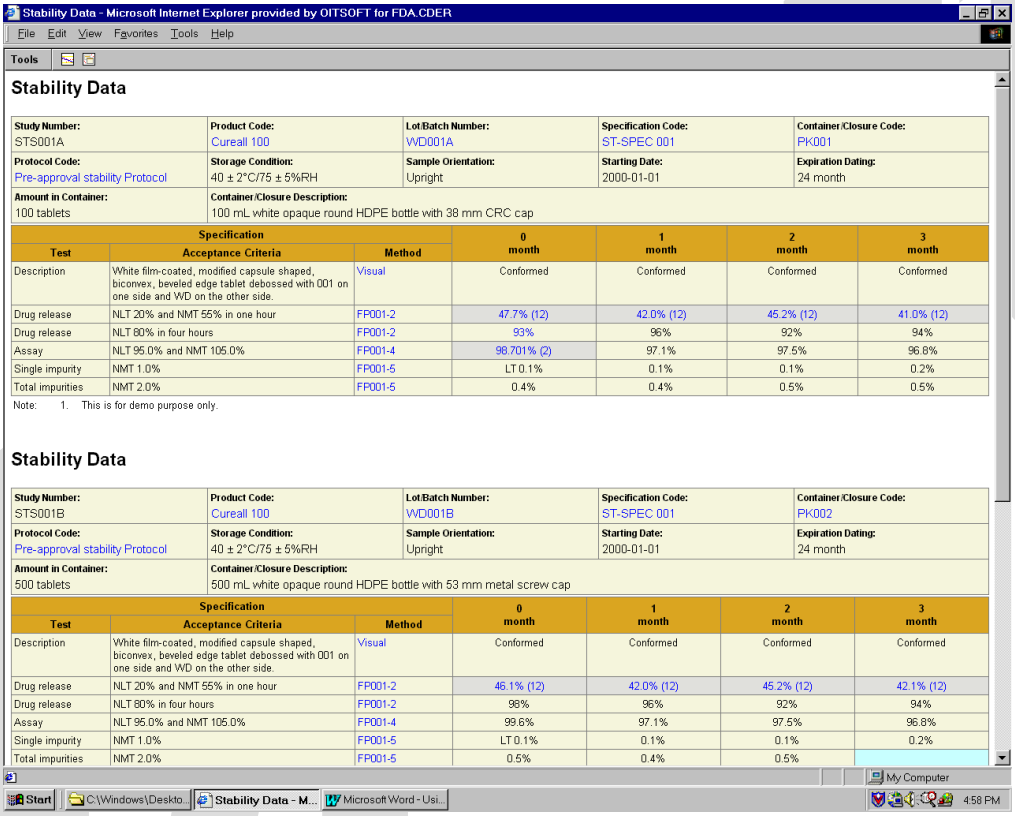
You need to have Internet Explorer (IE) version 5.5 installed to use this model. Some service releases (SR) of IE 5.0 will work (SR 500.2314.1003 will not work)

Default Data Presentation

You can start the Stability Review Tool by double clicking on the shortcut called "Click here for the stability review tool working model." on the following web page:

http://www.fda.gov/cder/ondc/presentations/stability/

You should see something that looks like the following picture:



Notice that this is a stability data table in the style recommended in CDER CMC guidance documents. In this picture there is a complete stability study and part of another with a scroll bar to bring up the parts you cannot see. The sections of the stability study table will be discussed below:

Stability Study Information

In the top three rows of the table the stability study is described. Information regarding the product, batch, specification, container closure, storage conditions, start date, duration and stability protocol are provided. Some of the information is colored blue. The blue text indicates a hyperlink to additional information.

Specification Section

The first cell in the fourth row spans three columns below it. These three columns contain the specification for this stability study. The three columns of the specification contain, from left to right, the test name, acceptance criteria, and the hyperlinked identification of the analytical procedure. The hyperlink opens a file containing the complete analytical procedure (these files are for demonstration so they have no content).

Data Report Section

To the right side of the Specification Section is the Data Report Section. The top row of the Data Report Section contains the sampling time points for the stability study. This study has only 4 sampling points. If you scroll to the last study, it has more.

Some of the data cells are shaded gray and have more than one number in them. This indicates the first number is a calculated average. The second number in parenthesis reports the number of samples used to create the average. If you click on these numbers another screen will "pop-up" and display all the data points along with the calculated high, low, average and RSD. All shaded gray cells indicate calculated results that were not directly reported.

In the third row of data under the 0 month sample time (Drug release test) there is a single number that is colored blue. Blue color on a directly reported data point indicates that there is a hyperlink to more information about the sample point.

Missing Data

If you scroll down to the second stability data report one of the data cells has no number in it and it is colored light blue. This is to draw your attention to the fact that no data is reported for this test and time point.

Tools

Graph Tool

At the top of the display there is a tool bar with two buttons on it. The left button is a graphing tool that requires you have Microsoft Excel ® installed to work properly. This documentation describes using Microsoft Excel 97 ® SR 2.

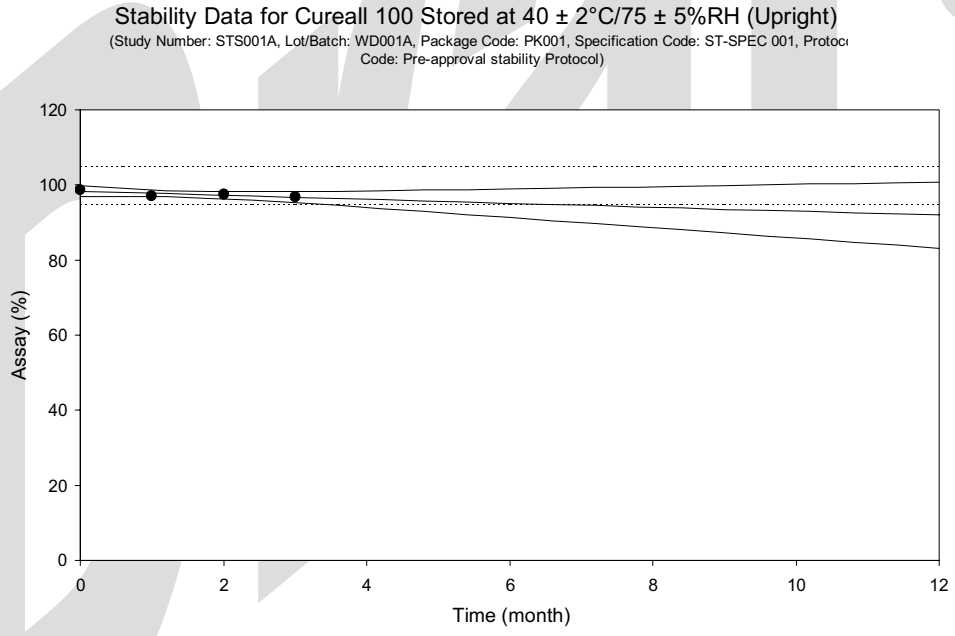
This tool requires a custom security setting in the browser. You should make http://www.fda.gov/cder/ondc/presentations/stability/ a trusted web site. To do that follow the following steps:

1. Click "Tools" on your browser toolbar to open the "Tools Pull-Down"
2. Click on "Internet Options…"
3. Click on the "Security" tab
4. Click on the icon named "Trusted Internet Sites"
5. Click on the "Sites…" button

6. Remove the check from the checkbox called "Require server verification (https:) for all sites in this zone"
7. Type the following into the box called "Add this Web site to the zone:" : http://www.fda.gov/cder/ondc/presentations/stability/Click "ok"
8. Click "ok" again

You are now ready to run the graph tool.

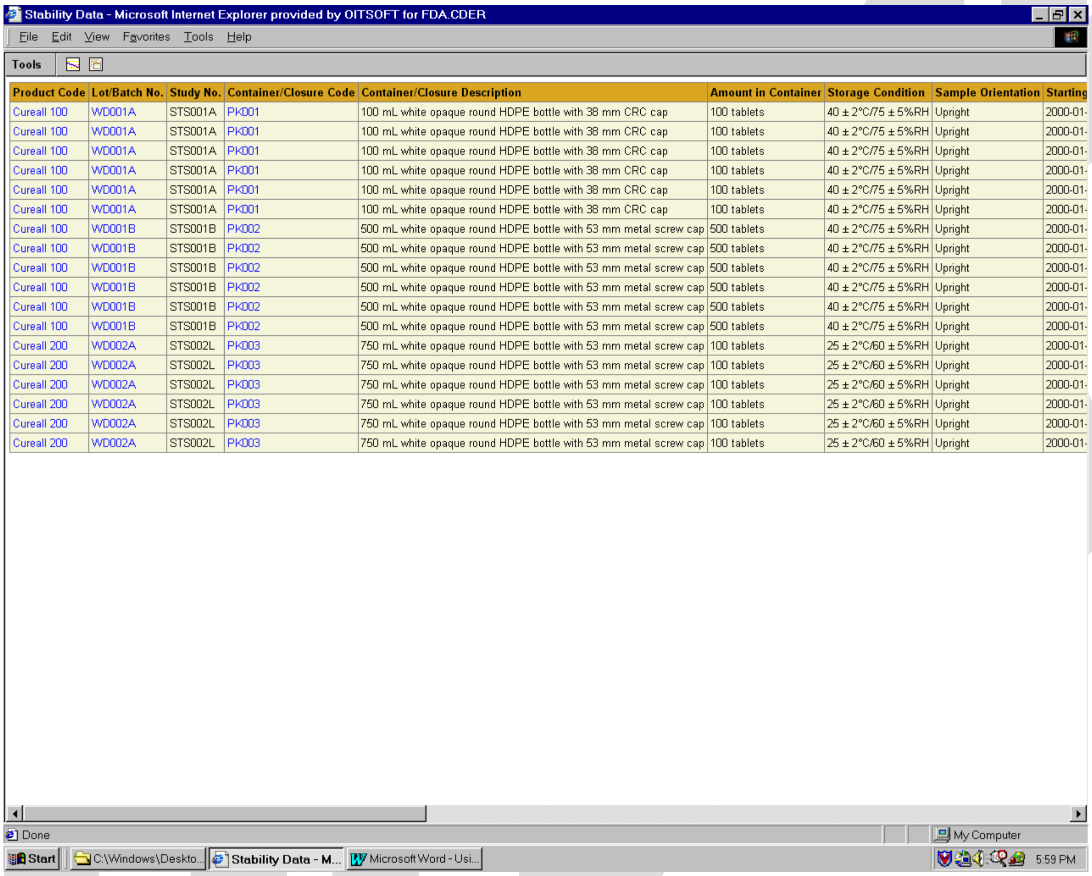
Click on the Stability Data Review Tool Toolbar button that is on the left and you should see a form pop-up and some check boxes appear to the left of the stability data table data rows. You should choose from the options: graph the trend line, the acceptance criteria that are being reported, and the 95% confidence bounds. You should also choose if you want to extrapolate the data and extend each of the graphed lines and curves to a time point specified by you. You should choose the test results you wish to graph by checking the box to the left of the test data row (You cannot select a row that does not have numeric data). For this documentation I chose to graph all the lines and curves, extrapolation to 12 (time units are provided by the data file) and I chose the assay test. The result is pictured below (if you set the "Initialize and script ActiveX controls not marked as safe" to "prompt" you will first see a prompt to which you should answer "yes"):



The dotted lines are the criteria limits provided in the data. The large dots are the actual data. The straight line is the calculated trend line and the curves are the calculated 95% confidence bounds.

Slice and Dice Tool

You may want to examine all the stability data in all the reports for a single test, container closure system or some other feature of the product. For this you use the slice and dice tool. Click on the right hand tool bar button and you should get something that looks like the following picture:



Product Code	Lot/Batch No.	Study No.	Container/Closure Code	Container/Closure Description	Amount in Container	Storage Condition	Sample Orientation	Starting
Cureall 100	WD001A	STS001A	PK001	100 mL white opaque round HDPE bottle with 38 mm CRC cap	100 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001A	STS001A	PK001	100 mL white opaque round HDPE bottle with 38 mm CRC cap	100 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001A	STS001A	PK001	100 mL white opaque round HDPE bottle with 38 mm CRC cap	100 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001A	STS001A	PK001	100 mL white opaque round HDPE bottle with 38 mm CRC cap	100 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001A	STS001A	PK001	100 mL white opaque round HDPE bottle with 38 mm CRC cap	100 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001A	STS001A	PK001	100 mL white opaque round HDPE bottle with 38 mm CRC cap	100 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001B	STS001B	PK002	500 mL white opaque round HDPE bottle with 53 mm metal screw cap	500 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001B	STS001B	PK002	500 mL white opaque round HDPE bottle with 53 mm metal screw cap	500 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001B	STS001B	PK002	500 mL white opaque round HDPE bottle with 53 mm metal screw cap	500 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001B	STS001B	PK002	500 mL white opaque round HDPE bottle with 53 mm metal screw cap	500 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001B	STS001B	PK002	500 mL white opaque round HDPE bottle with 53 mm metal screw cap	500 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 100	WD001B	STS001B	PK002	500 mL white opaque round HDPE bottle with 53 mm metal screw cap	500 tablets	40 ± 2°C/75 ± 5%RH	Upright	2000-01-
Cureall 200	WD002A	STS002L	PK003	750 mL white opaque round HDPE bottle with 53 mm metal screw cap	100 tablets	25 ± 2°C/60 ± 5%RH	Upright	2000-01-
Cureall 200	WD002A	STS002L	PK003	750 mL white opaque round HDPE bottle with 53 mm metal screw cap	100 tablets	25 ± 2°C/60 ± 5%RH	Upright	2000-01-
Cureall 200	WD002A	STS002L	PK003	750 mL white opaque round HDPE bottle with 53 mm metal screw cap	100 tablets	25 ± 2°C/60 ± 5%RH	Upright	2000-01-
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Cureall 200	WD002A	STS002L	PK003	750 mL white opaque round HDPE bottle with 53 mm metal screw cap	100 tablets	25 ± 2°C/60 ± 5%RH	Upright	2000-01-
Cureall 200	WD002A	STS002L	PK003	750 mL white opaque round HDPE bottle with 53 mm metal screw cap	100 tablets	25 ± 2°C/60 ± 5%RH	Upright	2000-01-

This is a simple table containing all the information for in the Stability Data File. Move the bottom scroll bar to the right and you can see the actual reported data points.

Removing Columns and Rows

Right mouse click while the cursor is on the table and a form will pop-up that provides you with instructions for removing columns and rows.

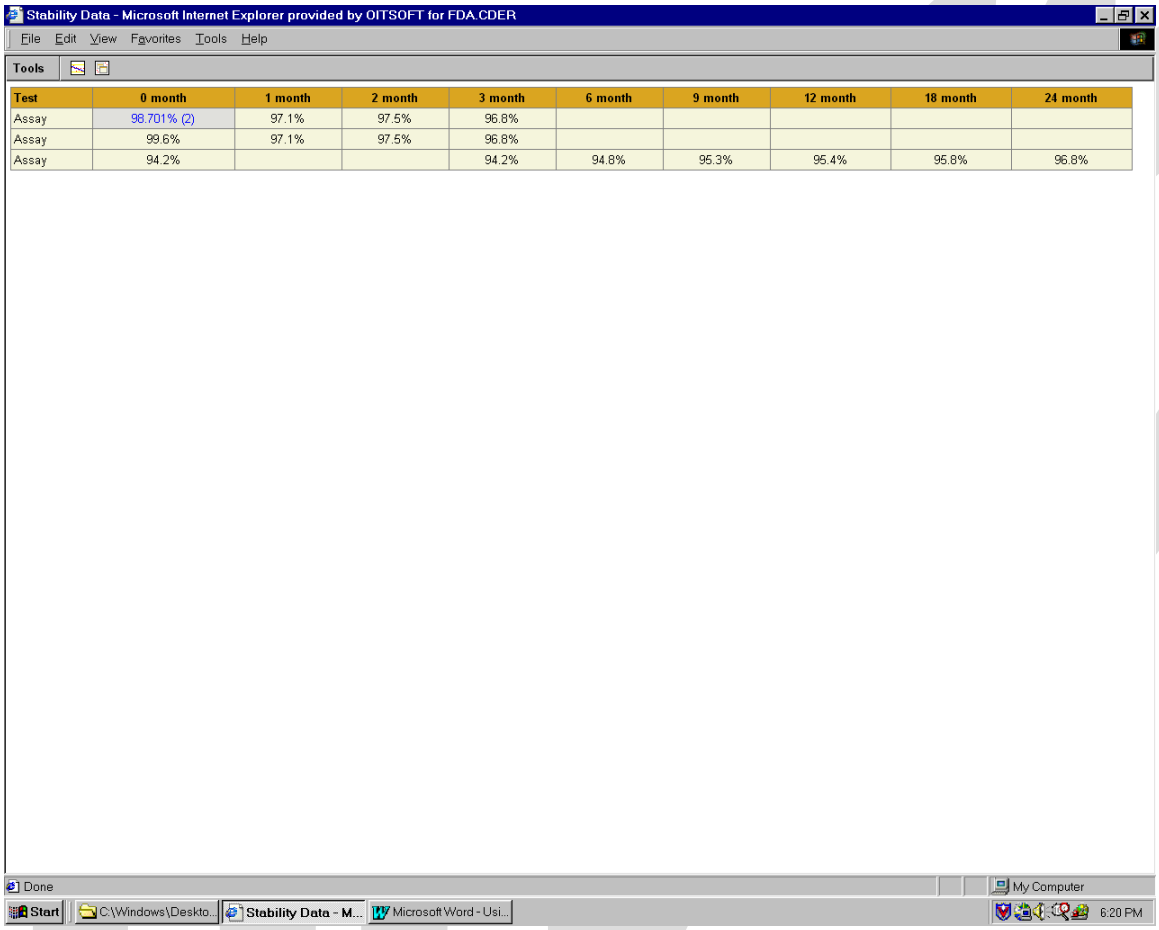
Click left mouse button on a cell to alter row display setting

Click right mouse button on a cell to alter coloumn[sic] display setting

Place the mouse on any cell when this form is displayed then right click and left click and its row and column will be shaded gray. Click the "OK" button and the rows and columns that are shaded gray are removed from the table. If you don't like what you see, right click to bring up the form and click on "reset" and all the modifications are removed. If you want to remove more

that one column or row at a time, hold down the control key "Ctrl" and when you click on the second column or row all the columns or rows between the first one and the second one will also be shaded.

Using this I was able to isolate all the assay tests for all the studies and display only the test name and the data. The result is in the following picture:



Test	0 month	1 month	2 month	3 month	6 month	9 month	12 month	18 month	24 month
Assay	98.701% (2)	97.1%	97.5%	96.8%					
Assay	99.6%	97.1%	97.5%	96.8%					
Assay	94.2%			94.2%	94.8%	95.3%	95.4%	95.8%	96.8%

Notice that the tool bar is still available if you want to graph any of these test results.

Contact Information

If you have questions, comments or would like to support development of this standard for reporting stability data please contact Jon Clark at the following address:

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